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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/367,052	08/06/1999	TADAMITSU KISHIMOTO	1422-386PCT	3818

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 02/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/367,052	KISHIMOTO ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,16,22 and 24-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,16,22 and 24-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 August 1999* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1-19-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Currently, claims 13, 16, 22, 24-35 are pending in the application.

2. In the prior action, mailed on June 15, 2004, claims 13, 16, and 22, and 24-35 were rejected. In the Response filed on September 15, 2004, the Applicant amended claims 13, 16, 22, 24-27, 29, 32, and 35.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on January 19, 2005, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

Specification

4. **(Prior Objection- Withdrawn)** The disclosure was objected to because of the following informalities: the discussions of the sequences on pages 10-12, 18-20, 22-23, 28, 41-44, and 46-50 of the specification appear to be misidentifying the sequences being discussed. In view of the amendment of the application to correct the sequence identifier numbers, the objection is withdrawn.

Claim Objections

5. **(New Objection)** Claims 13, 16, and 22 objected to because of the following informalities: the claims refer to the HIV-1 envelope protein (glycoprotein) by its abbreviation "env" without first identifying it by its complete name. It is suggested that the first instance of

the use of "env" in each claim (claim set) be amended to first introduce the protein by its complete name: e.g. "HIV-a envelope protein (env)." Appropriate correction is required.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. **(Prior Rejection- Maintained)** Claims 13, 16, 22, 24, 25, 27-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims were rejected because as indefinite as it is not known what activities fall within the scope of "an activity of a receptor capable of binding to a murine PBSF/SDF-1." The Applicant has amended the claims so as to include an additional functional requirement. However, the claims still include the rejected phrase. Because it is not clear what activity or activities may be present, and therefore what polypeptides may fall within the scope of the claim, the rejection is maintained.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. **(Prior Rejection- Maintained)** Claims 13, 16, 22, 24-27, 29, 31, 32, 34, and 35 were rejected in the prior action under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in

the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claims were rejected because the Applicant has not provided sufficient written description support for the claims as they are directed to (host cells comprising) DNAs encoding, or methods of using such to produce, a polypeptide with an activity of the murine receptor capable of binding PBSF/SDF-1, wherein the DNAs include derivatives or fragments of the DNA encoding the polypeptide of SEQ ID NO: 2. It is noted that the claims have been amended to add an additional functional requirement- that the encoded polypeptides have the activity of acting as a binding site for T-cell-line-tropic HIV-1 env cell line membrane fusion with a T-cell-line-tropic HIV-1 in the presence of human CD4.

The Applicant traverses the rejection on the grounds that the claims have been amended to exclude reference to SEQ ID NOs: 3 and 7, and that they have been amended to include the additional activity indicated above. These arguments are not found persuasive. It is first noted that each instance of reference to SEQ ID NOs: 3 or 7 have not been deleted from the claims. Further, even if specific reference to these sequences had been deleted, the claims still read on the rejected subject matter; i.e., any fragment or derivative of SEQ ID NO: 1 (or SEQ ID NO: 5) that has the required activity. Thus, the argument is not found persuasive.

While the Applicant has shown that SEQ ID NO: 1 and SEQ ID NO: 5 have the activity of binding to a murine PBSF/SDF-1, the Applicant has not shown 1) what activities are performed by the murine receptor, 2) what fragments or regions of the receptor are required to perform these activities, or 3) any fragments or derivatives which perform any such activities other than SEQ ID NO: 5 which has only been shown to effect binding to a murine PBSF/SDF-1,

and has not been demonstrated to perform any other activity, including the newly added activity as permitted fusion between a T-cell-line-tropic HIV-1 env cell line membrane fusion with a T-cell-line-tropic HIV-1 in the presence of human CD4. Thus, the current claim amendments have not overcome the rejection because they do not demonstrate possession of the claimed genus of polynucleotides which encode SEQ ID NO: 1, or any fragment or derivative that is able to perform the required functions (or to methods of using such polynucleotides to make polypeptides). The rejection is therefore maintained for the reasons above, and the reasons of record.

10. **(Prior Rejection- Maintained)** Claims 13, 16, 22, 24-27, 29, 31, 32, 34, and 35 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising the full sequence of SEQ ID NO: 1, does not reasonably provide enablement for embodiments comprising only fragments of or comprising derivatives of the sequence that encode polypeptide capable of binding to murine PBSF/SDF-1. As indicated above, the claims have been amended such that they further require that the claimed (host cells comprising) polynucleotides, or the polynucleotides used in the claimed methods, to act as a binding site for T-cell-line-tropic HIV-1 env cell line membrane fusion with a T-cell-line-tropic HIV-1 in the presence of human CD4. The claims have also been amended to delete specific reference to SEQ ID NOs: 3 and 7. The Applicant asserts that this amendment overcomes the rejection.

However, the rejection was not basis solely on the reference to these two sequences. The claims were also rejected for reading broadly on embodiments comprising any fragment or

derivative of the protein encoded by SEQ ID NO: 1 that has the indicated functions. The claims still read on such derivative or fragments, although the Applicant has presented no arguments or evidence that the application has enabled those in the art to make and use the full scope of the claims. Additionally, it was also noted that, while the Applicant has shown that "even the polypeptide encoded by SEQ ID NO: 5 has been shown to possess only one of the potential activities of the receptor" (i.e. the ability to bind to PBSF/SDF-1. There has been no showing that the ability to bind PBSF/SDF-1 is itself sufficient to also demonstrate the ability to facilitate T-cell-line-tropic HIV-1 env mediated cell fusion, or infection of a cell by the virus in the presence of hCD4. Because there has been no effort to address these additional concerns, the rejection is maintained for the reasons of record.

11. **(Prior Rejection- Withdrawn)** Claims 13, 16, 22, 31, 34, and 35 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement The claim read on a DNA capable of hybridizing under stringent conditions to a DNA encoding a polypeptide that binds to PBSF/SDF-1, and that simultaneously encodes for a polypeptide having the activity of binding to such a polypeptide. In view of the amendment of the claims such that they now read on DNA that hybridizes to the complements of the coding polynucleotides, the rejection is withdrawn.

12. **(Prior Rejection- Maintained)** Claims 22, 26,32, 34, and 35 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while potentially being enabling for a kit for the detection of HIV-1 infection comprising a cell transfected with a polynucleotide encoding CXCR-4 and CD4, does not reasonably provide enablement for a kit for the detection of the

onset of AIDS, or for kits for detecting HIV infection wherein the cells express CD4, and only a portion of the CXCR-4 receptor that binds to murine PBSF/SDF-1. The Applicant asserts that the amendment of the claims to delete reference to SEQ ID NOs: 3 and 7 overcomes the rejection. It is noted that the claims have also been amended to add the additional functional language described above.

The Applicant's argument that the deletion of reference to SEQ ID NOs: 3 and 7 is not found persuasive. As described in the prior action, the rejection was not based solely on the lack of evidence that these sequence bind to murine PBSF/SDF-1. In the action, it was additionally noted that the Applicant has not provided evidence that the ability of SEQ ID NO: 5 to bind to murine PBSF/SDF-1 is indicative of its ability to act as a co-receptor for HIV infection, and therefore sufficient to allow the claimed kit to operate. The Applicant has presented no arguments or evidence in response to the additional concerns identified in the rejection. The rejection is therefore maintained.

13. **(Prior Rejection-Maintained, and extended as Necessitated by Amendment)** Claims 16, 25, 29, and 30 were rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for cells recombinantly expressing hCD4 and mCXCR-4 that may be infected with T-cell-line-tropic HIV, does not reasonably provide enablement for any cell expressing hCD4 and mCXCR-4 and which may be infected by any HIV when contacted therewith. It is noted that claim 31 was mistakenly left out of the listing of the claims previously rejected. As this claim is dependant on claim 16, its inclusion in the rejection raises no new issues. The rejection is therefore extended to these claims for the reasons of record.

The Applicant argues that the amendment of the claims to refer to only T-cell0line-tropic HIV has overcome the rejection. However, while the amendment overcomes one ground of rejection, the rejection was also on the basis that the Applicant is not enabled for methods/cells involving any cell that expresses both hCD4 and mCXCR-4. It was specifically stated that, "the specification, while being enabling for cells recombinantly expressing hCD4 and mCXCR-4 ...[the specification] does not reasonably provide enablement for any cell expressing hCD4 and mCXCR-4." The Applicant has made no effort to respond to this portion of the rejection. The rejection is therefore maintained on this basis.

It is noted that the Applicant previously overcame a substantially identical rejection with respect to claim 22 by requiring that the cell express "heterologous hCD4 and mCXCR-4." Thus, such an amendment would also avoid the present rejection.

14. **(Prior Rejection- Maintained and extended as Necessitated by Amendment)** Claim 35 rejected was under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. This claim reads on methods of producing a polypeptide having "an activity of a receptor capable of binding to a murine PBSF/SDF-1" through expression of a vector encoding such polypeptide in a recombinant cell, wherein the "polypeptide supports cell membrane fusion mediated by a T-cell-line-tropic HIV-env and infection with a T-cell-line-tropic HIV-1." Claims 13, 16, 22, and 24-34 have been amended to include similar language (either directly, or through amendment of a claim from which the claim depends). The rejection is therefore extended to these amended claims.

Claim 35 was rejected for two reasons. First, the claim was rejected because it was not demonstrated that the presence of only the murine receptor would be sufficient to permit cell membrane fusion between mediated by a T-cell-line-tropic HIV-env and infection with a T-cell-line-tropic HIV-1. The Applicant has overcome this portion of the rejection through the amendment of the claim requiring the presence of human CD4.

However, the claim was also rejected because the Applicant has not demonstrated that any cell that expresses both hCD4 and murine CXCR-4 would have the indicated functional activities. I.e., the Applicant did not establish that the any cell expressing both hCD4 and mCXCR-4 would be capable of inducing cell membrane fusion mediated by a T-cell-line-tropic HIV-1 env. The Applicant has presented no persuasive argument or evidence with respect to this issue. The rejection is therefore maintained.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

16. **(Prior Rejection- Maintained)** Claims 13, 24, 25, 27-30, and 35 were rejected under 35 U.S.C. 102(a) as being anticipated by Nagasawa et al., PNAS 93: 14725-29 (of record in the IDS of August 6, 1999). The reference discloses the isolation of DNA encoding for the murine CXCR-4 receptor, and the cloning and transfection of CHO cells therewith. See, pages 14726-28. Thus, the reference teaches the currently claimed invention.

The Applicant has amended the claims to read on cells "expressing" rather than "comprising" the human CD4 and the murine CXCR-4 receptors. However, it is not clear how one cell differs structurally from the other. Additionally, it is noted the Nagasawa indicates that the murine T cells referred to on page 14729, which express the murine co-receptor, expressed the human CD4. Thus, the Applicant's argument that the amendment of the term "comprising" to "expressing" the human receptor is not found persuasive. The rejection is therefore maintained for the reasons of record, and the reasons above.

17. **(Prior Rejection- Maintained)** Claims 13, 16, 24, 25, 28, 30, and 35 were rejected under 35 U.S.C. 102(a) as being anticipated by either of Heesen et al. (supra), or Ashorn et al., J Virol 64: 2149-56. These claims read on a cell expressing the receptor encoded by the polynucleotide of claim 1, and a CD4 receptor. The Applicant traverses this rejection on what appears to be the same grounds as argued with respect to the Nagasawa reference above (i.e. the amendment of the claims to read on cells "expressing" rather than on cells "comprising" the human CD4). However, as each of these references teaches the same cells, and Ashorn teaches (see abstract) that the cells express the human receptor, the Applicant's argument is also not found persuasive with respect to these references. The rejection is therefore maintained for the reasons above, and the reasons of record.

It is again noted that the rejection of claim 22 was overcome by amending the claims to read on cells that exogenously express both hCD4 and mCXCR-4.

Conclusion

18. No claims are allowed.

19. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

James C. Housel 2/18/05

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